In the Specification

Please replace the paragraph beginning on page 7, line 15, with the following paragraph:

As new protease inhibitors are developed, the ability of certain amino acid substitutions to confer resistance to the inhibitor is usually determined by several methods, including selection of resistant strains in vitro, site-directed mutagenesis, and determination of amino acid changes that are selected during early phase clinical trials in infected patients. While some amino acid substitutions are specifically correlated with resistance to certain protease inhibitors (see below), there is considerable overlap between sets of mutations implicated in resistance to all approved protease inhibitors. Many investigators have attempted to classify these mutations as either being "primary" or "secondary", with varying definitions. For example, some investigators classify as primary mutations which are predicted, based on X-ray crystallographic data, to be in the enzyme active site with the potential for direct contact with the inhibitor. (e.g. D30N, G48V, I50V, V82A/F/S/T, I84V, N88S, L90M). Secondary mutations are usually considered as being compensatory for defects in enzyme activity imposed by primary mutations, or as having enhancing effects on the magnitude of resistance imparted by the primary mutations (e.g. L10I/F/R/V, K20I/M/R/T, L24I, V32I, L33F/V, M36I/L/V, M46I/L/V, I47V, I54L/V, L63X, A71T/V, G73A/S/T, V77I, N88D). Lists of mutations and corresponding inhibitors are maintained by several organizations, for example: Schinazi et al., Mutations in retroviral genes associated with drug resistance, *Intl. Antiviral News* 1999,7:46-69 and Shafer et

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al., Human Immunodeficiency Virus Reverse Transcriptase and Protease Sequence Database, Nucleic Acids Research 1999, 27(1), 348-352.

Please replace the paragraph beginning on page 32, line 1, with the following paragraph:

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Figs. 3a-3c
Examples of phenotypic drug susceptibility profiles. Data are analyzed by plotting the percent inhibition of luciferase activity vs. log10 concentration. This plot is used to calculate the drug concentration that is required to inhibit virus replication by 50% (IC50) or by 95% (IC95). Shifts in the inhibition curves towards higher drug concentrations are interpreted as evidence of drug resistance. Figure 3a shows the typical curve of drug susceptibility for the nucleoside reverse transcriptase inhibitor AZT. Figure 3b shows the typical curve of drug susceptibility for the non-nucleoside reverse transcriptase inhibitor efavirenz. Finally, Figure 3c shows the typical curve of drug susceptibility for the protease inhibitor indinavir. A reduction in drug susceptibility (resistance) is reflected in a shift in the drug susceptibility curve toward higher drug concentrations (to the right) as compared to a baseline (pre-treatment) sample or a drug susceptible virus reference control, such as pNL4-3 or HXB-2, when a baseline sample is not available.

Please replace the paragraph beginning on page 32, line 20, with the following paragraph:

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Figs. 4a-e
Phenotypic PRI susceptibility profile: patient 0732. A

PCR-based phenotypic susceptibility assay was carried out giving the phenotypic drug susceptibility profile showing decreased susceptibility to nelfinavir and indinavir, and increased susceptibility amprenavir. Figure 4a shows a dose response relationship in subjects treated with saquinavir. Figure 4b shows a dose response relationship in subjects treated with indinavir. Figure 4c shows a dose response relationship in subjects treated with ritonavir. Figure 4d shows a dose response relationship in subjects treated with nelfinavir. Finally, Figure 4e shows a dose response relationship in subjects treated with amprenavir.

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Please replace the paragraph beginning on page 32, line 27, with the following paragraph:

Figs. 5a-e

Phenotypic PRI susceptibility profile of a protease mutant generated by site-specific oligonucleotide-directed mutagenesis. A PCR-based phenotypic susceptibility assay was carried out giving the phenotypic drug susceptibility profile of a virus having substitutions at codons 63, 77, and 88 (L63P, V77I, and N88s). The profile demonstrated resistance to both nelfinavir and indinavir, and increased susceptibility to amprenavir. Figure 5a shows a dose response relationship in subjects treated with saquinavir. Figure 5b shows a dose response relationship in subjects treated with indinavir. Figure 5c shows a dose response relationship in subjects treated with ritonavir. Figure 5d shows a dose response relationship in subjects treated with nelfinavir. Finally, Figure 5e shows a dose response relationship in subjects treated with amprenavir.

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